

Ministry of health of the Republic of Belarus
Educational institution
«Gomel State Medical University»

Department of general and clinical pharmacology

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METHODOLOGICAL RECOMMENDATIONS

for a practical lesson on the discipline "Pharmacology"
for the third-year students of the Faculty of Foreign Students,
studying at the specialty 1-79 01 01 "General medicine"

TOPIC 33: «ANTINEOPLASTIC AGENTS»

Time: 3 hours

Approved at the meeting of the department of general and clinical pharmacology
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LEARNING AND EDUCATIONAL GOALS, OBJECTIVES, MOTIVATION FOR LEARNING THE TOPIC

Malignant neoplasms are one of the main causes of death worldwide. Every year about 7.6 million people die of this pathology. According to WHO, oncological diseases occupy 13% of the total mortality in the world. At the same time, 70% of all people who die of cancer live in countries with low per capita income. According to experts, the statistics of malignant neoplasms morbidity will remain disappointing in the nearest future. In particular, by 2030 the total number of deaths from this pathology will be 13 million.

Antiblastomics application in the treatment of malignant tumors can be both the main method of treatment (reticulosarcoma, malignant diseases of hematopoietic tissue, etc.) and an important component of complex therapy of patients with cancer along with surgical treatment and radiotherapy. Knowledge of pharmacology of anticlastic agents with taking into account their large arsenal is necessary for modern doctor in order to choose them rationally and apply them timely and correctly.

Learning objective:

Formation of scientific knowledge of the main pharmacological effects, providing therapeutic and preventive effect of drugs on the topic of class, indications and contraindications for their use, the issues of interaction of drugs, their combined use, for use in medical and preventive activities.

Educational purpose:

- to develop their value-personal, spiritual potential, to form the qualities of a patriot and citizen, ready for active participation in the economic, industrial, socio-cultural and public life of the country; to realize the social importance of their future professional activities, to learn to comply with academic and labor discipline, standards of medical ethics and deontology.

Tasks:

As a result of the study lesson, the student should

know:

- classification and basic characteristics of the studied drugs, pharmacodynamics and pharmacokinetics, indications and contraindications for their use, side effects;
- features of pharmacokinetics and pharmacodynamics, advantages and disadvantages of different dosage forms of these drugs;
- principles of research and testing of new drugs; information and reference and search systems;

be able to:

- analyze the effect of the studied drugs on the set of their pharmacological properties and the possibility of their use in medical practice; to write them in prescriptions;
- use different dosage forms of these drugs, based on the peculiarities of their pharmacodynamics and pharmacokinetics;
- work with scientific literature, search for information about the use and action of the studied drugs;

possess:

- skills in choice of drugs on the topic of the lesson;

- the rules of prescribing the studied drugs in the treatment of various diseases and pathological conditions, taking into account the indications;
- skills of dosage regime correction in case of pathological changes in functions of organs or systems responsible for biotransformation and elimination of drugs or in case of joint use of different drugs;
- skills to search, analyze and summarize information about the use and effects of the studied drugs.

Motivation for learning the topic:

- the specifics of training doctors in this specialty determines the need for students to purposefully study the main pharmacological effects, providing therapeutic and preventive effects of drugs on the topic of the class, indications and contraindications for their use, the interaction of drugs, their combined use, which will successfully complete the specialized disciplines of the specialty.

MATERIAL EQUIPMENT

Reference and informational literature, charts, tables, presentations, drug collections.

CONTROL QUESTIONS FROM RELATED DISCIPLINES

1. The specifics of prescribing different dosage forms. The concept of "absolute dose" and "relative dose". Rules for calculation of dosages depending on the age and body weight of the patient.
2. Phases of cell cycle. Theories of oncogenesis. Histology of tumors.
3. Basic biochemical and pathophysiological processes in the tumor cell.
4. Classification of tumors. Differences between malignant and benign tumors.

CONTROL QUESTIONS ON THE TOPIC OF THE CLASS

1. Principles of chemotherapy of malignant neoplasms. Definition and classification of anticlastic drugs.
2. Alkylating agents (cyclophosphamide, melphalan, busulfan), mechanism of action, peculiarities of the spectrum of antitumor activity, indications for use.
3. Antimetabolites (methotrexate, fluorouracil, cytarabine, mercaptopurine), mechanism of action, spectrum of antitumor activity, indications for use.
4. Mitosis-disrupting agents (vincristine, paclitaxel, etoposide, irinotecan), mechanism of action, spectrum of antitumor activity, indications for use.
5. Antitumor antibiotics (bleomycin, doxorubicin, mitomycin) mechanism of action, spectrum of antitumor activity, indications for use.
6. Enzyme agents (L-asparaginase), mechanism of action, spectrum of anti-tumor activity, indications for use.
7. Platinum drugs (cisplatin), hormonal drugs and their antagonists, mechanism of action, spectrum of antitumor activity, indications for use.
8. Peculiarities of pharmacology of antitumor agents of various chemical structures.
9. Radioactive isotopes and their use in oncology.
10. Complications of tumor chemotherapy, their prevention and treatment.

PROCESS OF THE STUDY

Theoretical part

Theoretical questions are described in the appendix to the methodological recommendations.

Practical part

1. Take notes on theoretical material demonstrated by the teacher.
2. Master the methods of solving the tasks and writing out prescriptions on the topic of the class.

Theme learning control

Conducted in the form of independent written work (solution of practical problems and prescriptions for individual task).

METHODOLOGICAL RECOMMENDATIONS FOR ORGANIZATION AND EXECUTION OF STUDENTS' INDEPENDENT WORK (SIW)

The time given for independent work can be used by students for:

- preparing for the practical classes;
- completing the tasks on the topic of the class in the workbook;
- preparing thematic reports, essays and presentations;
- taking notes from academic literature.

The main methods of organizing independent work:

- completing tests and practical tasks of the electronic educational-methodical complex (EEMC) for self-monitoring and self-assessment.

The list of tasks of the SIW:

- solving practical problems in the EEMC;
- completing the test tasks of the EEMC.

Control of the SIW is carried out in the form of:

- assessment of an oral answer to a question, report, report, or solution of a task in a practical class;
- individual conversation.

METHODOLOGICAL RECOMMENDATIONS FOR ORGANIZATION AND EXECUTION OF CONTROLLED INDEPENDENT WORK OF STUDENTS (CIWS)

Recommended forms of CIWS organization:

- doing exercises on the topic of the class in the workbook;
- writing an essay on a given topic;
- preparing a report and a multimedia presentation on a given topic.

The list of tasks of the CIWS:

Topics of essays / multimedia presentations:

1. Herbal remedies used for the treatment of oncological process (completion of workbooks).
2. ethical aspects of prescribing antitumor drugs to patients with oncologic pathology.

Forms of control of CIWS realization:

- checking and grading an essay on a given topic;
- checking and grading a multimedia presentation on a given topic.

LIST OF REFERENCES

1. Харкевич, Д. А. Фармакология : учебник для использования в учеб. процессе образоват. организаций, реализующих программы высш. образования по специальностям 33.05.01 "Фармация", 31.05.01 "Лечеб. дело", 31.05.02 "Педиатрия", 32.05.02 "Мед.-профилактич. дело", 31.05.03 "Стоматология" / Д. А. Харкевич. - 12 изд., испр. и доп. - Москва : ГЭОТАР-Медиа, 2017. - 754 с. : ил., табл., фот. - Рек. ФГАУ "ФИРО".
2. Конорев, М. Р. Курс лекций по фармакологии. В 2 т. Т. 2, ч. 1 : для студентов 3 и 4 курсов фармацевт. фак. учреждений высш. образования, обучающихся по специальности 1 - 79 01 08 "Фармация" / М. Р. Конорев, И. И. Крапивко, Д. А. Рождественский ; УО "ВГМУ", Каф. общей и клинической фармакологии с курсом ФПКипК. - Витебск: ВГМУ, 2019. - 294 с.: ил., табл. - Рек. УМО по высш. мед., фармацевт. образованию.
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4. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 курса лечебного., мед.-диагност., фак. подг. спец. для зарубеж. стран, 6 курса лечебного факультета и фак. подг. спец. для зарубеж. стран, аспирантов, магистрантов, учреждений мед. образования: в 2 ч. / Е. И. Михайлова [и др.]. – Гомель: ГомГМУ, 2019. – Ч. 1. – 56 с.
5. Кратко о лекарственных средствах: учебно – методическое пособие для студентов 3 курса лечебного., мед.-диагност., фак. подг. спец. для зарубеж. стран, 6 курса лечебного факультета и фак. подг. спец. для зарубеж. стран, аспирантов, магистрантов, учреждений мед. образования: в 2 ч. / Е. И. Михайлова [и др.]. – Гомель: ГомГМУ, 2019. – Ч. 2. – 84 с.

Antineoplastic agents (cont.) [1-14]

Classification	4.1 Hormonal agents				
	Glucocorticosteroids	Androgens	Estrogens	Gestagens	Gonadotropin-releasing hormone analogues
Drugs	1. Prednisolone 2. Hydrocortisone	3. Testosterone propionate	4. Phosphastrol 5. Extramustine	6. Megestrol 7. Medroxyprogesterone 8. Gepostet	9. Goserelin 10. Leuprolide
Mechanism of action	Reduce the production of gonadotropic hormones of the pituitary gland and the corresponding hormones of the gonads according to the feedback regulation → slowing the growth rate of hormone-dependent tumors				
Classification	4.2 Antihormonal agents				
	Adrenal cortex hormones antagonists	Antiandrogens	Antiestrogens	Aromatase inhibitors	
Drugs	11. Mitotane 12. Ketoconazole 13. Mifepristone	14. Cyproterone 15. Flutamide	16. Tamoxifen 17. Toremifene	18. Anastrozole 19.Exemistan	
Mechanism of action	Inhibit corresponding hormone receptors on tumor cells → slowing the growth rate of hormone-dependent tumors				
Pharmacological effects	1. Antiblast 2. Antiandrogenic (4-5, 14,15) 3. Androgenic (3) 4. Estrogenic (4,5) 5. Antiestrogenic (6-8,16,17,11-13) 6. Pharmacological castration (9,10)				
Side effects	1. Dyspepsia 2. Ulceration of the gastrointestinal mucosa (1-2) 3. Steroid diabetes mellitus (1-2) 4. Cushing's syndrome (1-2) 5. Virilization (3) 6. Gynecomastia (4-8, 14, 15) 7. Uterine bleeding (3-5,16-17) 8. Thrombosis (4-8)				
Indications	1. Leukemia (1-2) 2. Lymphomas (1-2) 3. Prostate cancer (4-8,10,15) 4. Breast cancer (3, 6-9, 16-19) 5. Uterine cancer (6-8, 16, 17) 6. Kidney cancer, nephroblastoma (Williams tumor) (16, 17) 7. Tumor of the adrenal cortex (11-13)				
Contraindications	1. Individual intolerance 2. Pregnancy and lactation 3. Severe liver and / or kidney dysfunction 4. Bone marrow hypoplasia 5. Acute infectious diseases 6. Ulcerative lesions of the gastrointestinal tract (1-2)				
NB!	1. Hormonal antimicrobial agents differ from cytostatics by significantly less toxicity 2. In hormone-dependent tumors, inhibition of the synthesis of a hormone or its action leads to a decrease or even a complete regression of the tumor				

Classification	5. Antibiotics		6. Enzymes	7. Substances of different chemical structure	8. Radioactive isotopes
Drugs	I generation anthracyclines 1. Doxorubicin (Adryblastin) 2. Daunorubicin	II generation anthracyclines 3. Epirubicin (Veroepirubicin) 4. Idarubicin (Vfend)	7. Asparaginase	8. Hydroxycarbamide (Hydroxyurea) 9. Procarbazine (Natulan)	10. Radium 11. Cobalt 12. Gold 13. Phosphorus 14. Iodine
	5. Bleomycin 6. Mitomycin				
Mechanism of actions	Bind to DNA → violation of DNA transcription → inhibition of RNA synthesis. Non-cyclo-specific, except bleomycin (specifically inhibits G2 phase).		Destruction of plasma asparagine → termination of protein synthesis → inhibition of tumor cells growth. Affect G1 phase.	Inhibition of the enzyme ribonucleotide → inhibition of DNA synthesis. Affect S phase.	The ionizing radiation → the formation of free radicals and oxidants → damage to the structure of DNA → the death of tumor cells.
Pharmacological effects	1. Antineoplastic 3. Cytotoxic 4. Cytostatic 5. Immunosuppressive 2. Antibacterial (1-6)				
Side effects	1. Nausea, vomiting 5. Neuritis, myalgia, arthralgia 2. Inhibition of bone marrow hematopoiesis 6. Hepatotoxicity 3. Alopecia 7. Nephrotoxicity 4. Cardiotoxicity (1-4)				
Indications	1. Thyroid gland tumors (1, 5, 14) 4. Tumors of the head and neck (1,3,5,8) 7. Brain tumors (1-5,8,10-12) 2. Hemoblastoses (1-4, 7, 8) 5. Testicular cancer (5,8) 8. Pulmonary cancer (1-3,5,8,10-12) 3. Sarcoma (1, 3) 6. Melanoma (1, 3, 8) 9. Stomach cancer (1,3,5,8,10-12) 10. Tumor diagnostics (10-14)				
Contraindications	1. Pregnancy 4. Severe impairment of liver and renal function 2. Lactation. 5. Bone marrow hypoplasia 1. Individual intolerance 6. Acute viral infections				
NB!	1. Dosage of cytostatics is based on the area of the body. 2. Cyclo-specific agents are used for rapidly growing tumors (leukemia, melanoma, sarcoma, etc.), non-cyclo-specific agents are effective in fast-and slow-growing tumors.				

Antineoplastic agents are drugs affecting the cell division. They damage the DNA and initiate apoptosis, preventing the development and spread of neoplastic cells [1-14]

Classification	1. Alkylating agents				
	Nitrogen mustards	Triazenes	Alkyl sulfonates	Nitrosoureas	Alkylating agents of a different chemical structure
Drugs	1. Cyclophosphamide (cytophosphane) 2. Chlorambucil (Leukeran) 3. Melphalan (Alkeran, Sarcolysin)	4. Dacarbazine 5. Temozolomide	6. Busulfan (Myleran)	7. Streptozocin 8. Lomustine 9. Carmustine 10.Thiophosphamide	11. Cisplatin 12. Pipobroman
Mechanism of action	Binding of alkyl groups to nucleic acids and proteins → fragmentation of DNA strands → Violation of the structure and function of DNA Affect all phases of the cell cycle.				
Classification	2. Antimetabolites			3. Plant alkaloids	
	Folic acid analogues	Purine analogues	Pyrimidine analogue	Vinca alkaloids	Taxanes Podophyllotoxins
Drugs	13. Methotrexate	14. Mercaptopurine	15. Fluorouracil	16. Vincristine 17. Vinblastine	18. Paclitaxel 19. Teniposide
Mechanism of action	Antagonists of natural cell components → inhibition enzymatic processes in the cell → violate the synthesis of nucleic acids. Cyclo-specific – specifically attack cells in a particular phase of the cell cycle (S phase)			Inhibit the division of tumor cells at various stages of mitosis. Cyclo-specific.	
Pharmacological effects	1. Antiblast 2. Cytotoxic 3. Cytostatic 4. Immunodepressive				
Side effects	1. Nausea, vomiting 3. Immunodepression 5. Neuritis, myalgia, arthralgia 7. Nephrotoxicity 2. Inhibition of bone marrow hematopoiesis 4. Alopecia 6. Hepatotoxicity				
Indications	1.Hemoblastoses (1-3,6,12,14,16,17) 3. Melanoma (4-5, 7-10,16) 5. Genital tumors (3,11, 16-19) 7.Brain tumors (7-10) 2.Myeloma disease (1, 3, 9) 4. Soft tissue sarcoma (4-5, 12, 16,17) 6. Colorectal cancer (4,5,15)				
Contraindications	1. Individual intolerance 3. Severe liver and / or kidney dysfunction 5. Acute infectious diseases 2. Pregnancy and lactation 4. Bone marrow hypoplasia				